

## PATENT COOPERATION TREATY

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## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

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<b>Date of mailing</b> (day/month/year) 10 August 1999 (10.08.99)	
<b>International application No.</b> PCT/US99/00465	<b>Applicant's or agent's file reference</b> KHGL-0001WO
<b>International filing date</b> (day/month/year) 08 January 1999 (08.01.99)	<b>Priority date</b> (day/month/year) 08 January 1998 (08.01.98)
<b>Applicant</b> HOFFMAN, Keith, B. et al	

1. The designated Office is hereby notified of its election made:

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in the demand filed with the International Preliminary Examining Authority on:

22 July 1999 (22.07.99)

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in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was☐

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 31/135</b>	<b>A1.</b>	<b>(11) International Publication Number:</b> <b>WO 99/34789</b> <b>(43) International Publication Date:</b> 15 July 1999 (15.07.99)
<b>(21) International Application Number:</b> PCT/US99/00465 <b>(22) International Filing Date:</b> 8 January 1999 (08.01.99)  <b>(30) Priority Data:</b> 60/070,736 8 January 1998 (08.01.98) US  <b>(71)(72) Applicants and Inventors:</b> HOFFMAN, Keith, B. [US/US]; 5110 San Aquamo Drive, San Diego, CA 92109 (US). LYNCH, Gary [US/US]; 4 Gibbs Court, Irvine, CA 92717 (US).  <b>(74) Agent:</b> FIELD, Bret, E.; Bozicevic, Field & Francis LLP, Suite 200, 285 Hamilton Avenue, Palo Alto, CA 94301 (US).		<b>(81) Designated States:</b> AU, CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> USE OF SERINE PROTEASE INHIBITORS TO INHIBIT PATHOPHYSIOLOGY AND NEUROPATHOLOGY IN A HOST  <b>(57) Abstract</b>  Methods are provided for inhibiting cell adhesion molecule cleavage in brain tissue of a host. In the subject methods, an effective amount of a protease inhibitor, particularly serine protease inhibitors, such as those that inhibit tPA and related proteases, is administered to the host. The subject methods find use in the treatment and prevention of pathophysiology and neuropathology in a host, such as the treatment of a variety of pathological conditions resulting from pathophysiology and/or excitotoxicity. Specific pathological conditions in which the subject methods find use include epilepsy (and related seizure states) and neuronal damage associated with excessive glutamate activity, e.g. resulting from an acute event such as hypoxia, head trauma or stroke.		

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/00465

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 31/135

US CL : 514/649

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/649

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
STN; COMPOUNDS AND METHODS OF USE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Chemical Abstracts, volume 121, number 13, issued 26 September 1994, FRIEDRICH, T. "Treatment of neurodegenerative diseases with thrombin inhibitors", page 117, abstract no. 149109s, Ger. Offen. DE 4,303,646, 11 August 1994, see entire abstract.	1-24
Y	Chemical Abstracts, volume 11, issued 13 SEPTEMBER 1982, PINSKY et al, "Peptidase inhibitors reduce opiate narcotic withdrawal signs, including seizure activity, in the rat." page 99, abstract no 85256p, Brain Res., Vol. 243(2), pages 301-307, see entire abstract.	1-24

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search

25 FEBRUARY 1999

Date of mailing of the international search report

23 MAR 1999

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**INTERNATIONAL SEARCH REPORT****International application No.**  
**PCT/US99/00465****C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

<b>Category*</b>	<b>Citation of document, with indication, where appropriate, of the relevant passages</b>	<b>Relevant to claim No.</b>
<b>Y</b>	<b>Chemical Abstracts, volume 76, number 11, issued 13 March 1972, KAZMIROWSKI et al, "Irreversible enzyme inhibitors", page 434, abstract no. 59218z, Ger. (East) 81,393, 20 April 1971, see entire abstract.</b>	<b>25</b>